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EXAMINER	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/713,790	PIER ET AL.	
	Examiner	Art Unit	
	S. Devi, Ph.D.	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 July 2010*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,4-7,9-21,23-25,42,86-91 and 93-99* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,4-7,9-21,23-25,42,86-91 and 93-99* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *04302010*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

RESPONSE TO APPLICANTS' AMENDMENT

Applicants' Amendment

1) Acknowledgment is made of Applicants' amendment filed 07/06/10 in response to the non-final Office Action mailed 01/05/10.

Status of Claim(s)

2) Claims 1, 2, 7, 9-11, 14-16, 20, 21, 25, 42, 86-91, 93-97 and 99 have been amended via the amendment filed 07/06/10.

Claims 8 and 92 have been canceled via the amendment filed 07/06/10.

Claims 1, 2, 4-7, 9-21, 23-25, 42, 86-91 and 93-99 are pending and are under examination.

Information Disclosure Statement

3) Acknowledgment is made of Applicants' information disclosure statement filed 04/30/10. The information referred to therein has been considered and a signed copy is attached to this Office Action.

Prior Citation of Title 35 Sections

4) The text of those sections of Title 35 U.S. Code not included in this action can be found in a prior Office Action.

Prior Citation of References

5) The references cited or used as prior art in support of one or more rejections in the instant Office Action and not included on an attached form PTO-892 or form PTO-1449 have been previously cited and made of record.

Rejection(s) Moot

6) The rejection of claim 8 made in paragraph 15 of the Office Action mailed 03/06/09 and maintained in paragraph 17 of the Office Action mailed 01/05/10 under 35 U.S.C § 112, first paragraph, as containing new matter, is moot in light of Applicants' cancellation of the claim.

7) The rejection of claim 92 made in paragraph 21(d) of the Office Action mailed 03/06/09 under 35 U.S.C. § 112, second paragraph, as being indefinite, is moot in light of Applicants' cancellation of the claim.

8) The rejection of claim 92 made in paragraph 23 of the Office Action mailed 03/06/09 under 35 U.S.C. 102(e)(2) as being anticipated by Joyce *et al.* (US 7,157,443), is moot in light of Applicants' cancellation of the claim.

9) The rejection of claim 92 made in paragraph 24 of the Office Action mailed 03/06/09 under 35 U.S.C. 102(a) as being anticipated by Yang *et al.* (*Tetrahedron Lett.* 43: 7561-7563, October 2002), is moot in light of Applicants' cancellation of the claim.

Rejection(s) Withdrawn

10) The rejection of claims 1, 21 and the dependent claims 4-7, 9-11, 14-18, 20, 23-25, 42 and 98 made in paragraph 15 of the Office Action mailed 03/06/09 and maintained in paragraph 17 of the Office Action mailed 01/05/10 and the rejection of claim 99 made in paragraph 17 of the Office Action mailed 01/05/10 under 35 U.S.C § 112, first paragraph, as containing new matter, is withdrawn in light of Applicants' amendment to the claims and/or the base claim.

11) The rejection of claims 23 and 24 made in paragraph 21(c) of the Office Action mailed 03/06/09 under 35 U.S.C. § 112, second paragraph, as being indefinite, is withdrawn upon further consideration.

12) The rejection of claims 23-25, 87-91 and 93-97 made in paragraph 21(d) of the Office Action mailed 03/06/09 under 35 U.S.C. § 112, second paragraph, as being indefinite, is withdrawn.

13) The rejection of claims 86, 88, 93-95 and 97 made in paragraph 23 of the Office Action mailed 03/06/09 under 35 U.S.C. 102(e)(2) as being anticipated by Joyce *et al.* (US 7,157,443, of record), is withdrawn in light of Applicants' amendment to the claims and/or the base claim. Applicants' acknowledgment that Joyce *et al.* report an SEA antigen SEA having 40-60% of R1 groups as H and the remainder of R1 groups being COCH3 and that the antigen of Joyce *et al.* may comprise 40-60% of R1 groups that are COCH3, has been noted.

14) The rejection of claim 19 made in paragraph 26 of the Office Action mailed 03/06/09 under 35 U.S.C § 103(a) as being unpatentable over Joyce *et al.* (US 7,157,443) as applied to claim 2, is withdrawn.

15) The rejection of claim 25 made in paragraph 24 of the Office Action mailed 03/06/09 under 35 U.S.C. 102(a) as being anticipated by Yang *et al.* (*Tetrahedron Lett.* 43: 7561-7563, October 2002), is withdrawn in light of Applicants' amendment to the claim.

16) The rejection of claim 42 made in paragraph 21(a) of the Office Action mailed 03/06/09 under 35 U.S.C. § 112, second paragraph, as being indefinite, is withdrawn in light of Applicants' amendment to the claim.

17) The rejection of claims 21, 86 and 87 made in paragraph 21(b) of the Office Action mailed 03/06/09 under 35 U.S.C. § 112, second paragraph, as being indefinite, is withdrawn in light of Applicants' amendment to the claims.

Rejection(s) Maintained

18) The rejection of claims 20, 42, 97 and 99 made in paragraph 19 of the Office Action mailed 03/06/09 under 35 U.S.C. § 112, first paragraph, as containing inadequate written description, is maintained for the reasons set forth therein and herein below.

Applicants cite case law and acknowledge that the written description requirement for a claimed genus may be satisfied by description of a representative number of species by an actual reduction to practice, or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus. Applicants assert that they have disclosed the relevant, identifying characteristics of the claimed genus and have demonstrated that such characteristics correlate with the functional characteristics of the claimed genus. Applicants state that the specification at lines 24-27 of page 2 has identified a deacetylated version of an isolated beta-l,6-glucosamine PNAG polymer, optionally conjugated to a carrier compound, that has less than 40% of its glucosamine amino groups substituted with acetate which is highly immunogenic *in vivo* and preferentially elicits antibodies that mediate opsonic killing and protection from infection. Applicants further assert that page 3, line 6 through page 5, line 21 of the specification teaches the structure of the isolated polymer, whether or not conjugated to a carrier compound. Applicants point to parts of the specification and state that the specification teaches pharmaceutical compositions, which 'may be used as vaccines', and that these compositions comprise the polysaccharide in an amount effective to stimulate an

immune response, such as an antigen-specific immune response. Applicants argue that the definition of 'vaccine' proffered by the Office is based, in part, on a definition of the term provided by the patent applicant in *In re Wright* and, as such, is not particularly relevant to the instant claims. Applicants submit that Example 6 and Figures 5-9 demonstrate that administration of the claimed isolated polysaccharide results in the production of opsonic antibodies that are able to kill staphylococcal strains more efficiently than antibodies produced following administration of highly acetylated forms of the claimed polysaccharide. Applicants further submit that one of ordinary skill in the art would reasonably conclude that the production of such opsonic antibodies within subjects receiving the claimed polymer or polysaccharide would lead to immunity in said subjects against bacteria that express PNAG. With these, Applicants conclude that the claimed deacetylated polysaccharides are shown in the specification to be more efficient than the highly acetylated polysaccharides at inducing higher titers of opsonic antibodies specific for PNAG. Applicants state that they have therefore clearly disclosed the structural feature that distinguishes the claimed polymers and polysaccharides from other polymers and polysaccharides and that correlates with the functional activity ascribed to the claimed polymers and polysaccharides. Applicants contend that the written description requirement does not require the existence of working examples, and assert that the instant working examples lead one of skill in the art to reasonably conclude that Applicants had possession of the claimed invention. Applicants allege that the Office provides no basis or support for the assertion that there is unpredictability relating to the solubility, immunogenicity, and immunospecific protective capacity of the claimed polymers and polysaccharides. Applicants argue that Maira-Litran's (*Infect. Immun.* 73: 6752-6762, 2005, of record) showing that certain species are most effective at bacterial killing does not establish

unpredictability with relation to the claimed genus. Applicants allege that the Office has provided no evidence that other species within the claimed genus are not efficacious. Applicants point to parts of the *post-filing publication* of Maira-Litran *et al.* and state that the reference supports the conclusion that antibodies reactive with the nonacetylated, backbone portion of the PNAG antigen were able to mediate clearance of bacteria from the blood and protection against a high-dose lethal infection, and that poorly acetylated forms of the vaccine are clearly capable of inducing the desired antibody.

Applicants' arguments have been carefully considered, but are not persuasive.

First, Applicants are correct in that a representative number of species have to be described in order to satisfy the written description requirement for a claimed genus. 'A patentee will not be deemed to have invented species sufficient to constitute the genus by virtue of having disclosed a single species when …. the evidence indicates that ordinary artisans could not predict the operability in the invention of any species other than the one disclosed'. *In re Curtis*, 354 F.3d 1347, 1358, 69 USPQ2d 1274, 1282 (Fed. Cir. 2004). For inventions in an unpredictable art, adequate written description of a genus embracing widely variant species cannot be achieved by disclosing only one species within the genus. See for example, *Eli Lilly*. The instant specification does not convey sufficiently detailed, relevant identifying characteristics of the presently claimed genus of deacetylated PNAG variants of the recited molecular weight, each having the recited requisite vaccine functions, described by Applicants as specific opsonic and bacterial killing functions, and the capacity to stimulate an immune response in a human or non-human subject against any species of *Staphylococci* and any genera of bacteria that make native PNAG. As set forth previously, the description of a single 15-20%

deacetylated polymer species within the claimed broad genus may not be sufficient to support the patentability of the vast genus having the requisite functions under 35 U.S.C § 112, first paragraph. See *University of California v. Eli Lilly & Co.*, 119 F.3d 15559, 1567, 43 USPQ2d 1398, 1405 (Fed. Cir. 1997). A sufficient number of representative species must be included 'to demonstrate that the patentee possesses the full scope of the [claimed] invention', which is lacking in the instant case. *Lizardtech, Inc. v. Earth Resource Mapping, Inc.*, 424 F.3d 1336, 1345, 76 USPQ2d 1724, 1732 (Fed. Cir. 2005). As ser forth previously, written description requires more than a mere statement that something is a part of the invention and a reference to a potential method for isolating it. See *Fiers v. Revel*, 25 USPQ2d 1601, 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016. Other than a purified staphylococcal dPNAG with 15-20% of acetate substitution, a representative number of such dPNAG having acetate substitutions encompassed within the recited broad range of zero to less than 40% has not been *correlated* with the *requisite* vaccine functions, i.e., staphylococcus-specific and non-staphylococcus-specific opsonic and bacterial killing, and the requisite broad immunoprotective specificity against any generic bacteria that make native PNAG or against any species of *Staphylococci* that make native PNAG. Without a concrete structure-function correlation, the claims do little more than define the claimed invention by function. That is not sufficient to satisfy the written description requirement. *Ex parte Kubin*, 83 USPQ2d 1410 (Bd. Pat. Appl. & Int. 2007) citing *Eli Lilly*, 119 F.3d at 1568, 43 USPQ at 1406 ('definition by function ….. does not suffice to define the genus because it is only an indication of what the gene does, rather than what it is'). Applicants were not in possession of a representative number of dPNAG-containing compositions or vaccines of varying degrees of acetate substitution spanning the broad range of 0 to less than 40%,

wherein the compositions or vaccines induced protective or opsonic antibodies against homologous or heterologous *Staphylococci* making native PNAG and against any other non-staphylococcal bacteria making native PNAG. This is critically important because the effect of 0%, 1-15%, or 20 to less than 40% acetate substitution on the immunogenicity, opsonogenicity, and/or immunospecific protection of isolated PNAG in human or non-human subjects, or in an art-accepted animal model, is not predictable. The precise degree of acetate substitution in dPNAG needed for the protective vaccine functions against staphylococci or non-staphylococci making native PNAG was neither known nor predictable *at the time of the invention*. The post-filing literature, cited herein to solely address Applicants' arguments, discloses the following. For example, with regard to the acetylation of PNAG as related to its protective efficacy, the reference of Gening *et al.* (*Infect. Immun.* 78: 764-772, 2009), published about seven years after the effective filing date of the instant application, teach that acetylated PNAG does not induce protective antibodies to PNAG. See abstract. Cerca *et al.* (*Infect. Immun.* 75: 3406-3413, 2007 – Applicants' IDS) teach that highly acetylated (>90%) PNAG conjugated to diphtheria toxoid induces antibodies that lacked protective efficacy against PNAG-positive *S. aureus* strains. In connection with this statement, Cerca *et al.* cite reference 29, i.e., Maira-Litran *et al.* (*Infect. Immun.* 73: 6752-6762, 2005, of record). Cerca *et al.* further mention of the work of Vuong *et al.* that antibodies raised against PNAG are not optimally protective in mice. See first full paragraph on page 3407. Cerca *et al.* show that there are multiple properties of PNAG which contribute to the pathogenesis of staphylococcal infections. See page 3412. Three years after the effective filing date of the instant application, Kelly-Quintos *et al.* (*J. Infect. Dis.* 192: 20, 2005) teach that 'the conjugation of highly acetylated PNAG' to a carrier protein 'does not elicit protective antibody'. See

lines 1 and 2 in right column on page 2018. With these, isolated PNAG species of at least 1200 Daltons having up to what degree of acetylation are considered highly acetylated and therefore not protective, and what degree of acetylation are optimally acetylated and therefore are optimally protective not only against staphylococci that produce native PNAG, but against the broadly recited non-staphylococcal bacteria that make native PNAG, was not known, and is not adequately described in the instant specification. Animal studies disclosed in the instant specification comparing the immunogenicity of highly acetylated PNAG with that of ~15% acetylated PNAG (dPNAG) conjugated to a protein carrier do not set an upper or lower limit of optimal deacetylation required for optimal protection and do not show possession of PNAG species of at least 1200 Daltons having an acetate substitution spanning the broad range of 0 to 15% and 16 to less than 40%, wherein the PNAG compositions or vaccines induce protective or opsonic antibodies against homologous or heterologous *Staphylococci* making native PNAG and against any other non-staphylococcal bacteria making native PNAG. This is critically important because even in 2010, about eight years after the effective filing date of the instant application, Gening *et al.* (*Infect. Immun.* 78: 764-772, 2010) teach that 'it was not clear from the prior vaccine studies if some level of acetylation on the glucosamine monomers was needed for the maximal protective immunity, or if some specific pattern of acetylation had to be maintained in order to produce a protective immune response'. See paragraph bridging pages 770 and 771 of Gening *et al.* Whether or not native PNAG served as a virulence factor and a protective antigen in every species of staphylococci and among the vast non-staphylococcal bacteria making native PNAG was neither known, nor predictable *at the time of the invention*. For example, with regard to immunization against *S. aureus* using PIA (incorrectly regarded as PNSG) at the time of the invention, Gotz (*Mol. Microbiol.*

43: 1367-1378, March 2002) taught that '[w]hether vaccination against *S. aureus* and *S. epidermidis* in the long run would be successful is questionable, especially as *S. aureus* produces numerous extracellular and surface-bound virulence factors, and *S. aureus* vaccination trials have a long tradition of failure – to date, no staphylococcal vaccine has found its way into practical application'. See first full paragraph on page 1374. Clearly, *at the time of the invention*, other than the composition species comprising a purified staphylococcal dPNAG species having 15-20% acetate substitution, wherein the dPNAG was conjugated to diphtheria toxoid or tetanus toxoid protein carrier species, which when administered to rabbits along with Freund's adjuvants induced opsonic antibodies to some specific *S. aureus* strains and a specific *S. epidermidis* strain (see Examples 2 and 4-6 and Figures 4-6 and 9), Applicants were not in possession, *at the time of the invention*, of a sufficient number of isolated species representative of the claimed broad genus of dPNAG polymers including those having a degree of acetylation beyond 20% up to 40% and below 15%, wherein the species are capable of serving as a vaccine capable of inducing protective opsonic antibodies either against homologous or heterologous *Staphylococcus aureus,* any species of *Staphylococcus,* or any other bacteria that produce acetylated, partially acetylated, deacetylated, or non-acetylated beta-1,6-glucosamine polysaccharide. Furthermore, Applicants were not possession of a less than 40% acetylated beta-1,6-glucosamine polysaccharide composition that stimulated an immune response against any bacteria, pathogenic or non-pathogenic, that comprised or expressed native PNAG. Contrary to Applicants' statement, one of ordinary skill in the art would not reasonably conclude that the production of opsonic antibodies by dPNAG within subjects receiving the claimed polymer or polysaccharide would lead to immunity in said subjects against bacteria that express PNAG. It is well known in the art that

whether or not a particular antigen stimulates an immune response and protects against homologous or heterologous pathogens is not a predictable event. For example, even three years after the effective filing date of the instant application, Kelly-Quintos *et al.* (*J. Infect. Dis*. 192: 2012-2019, 2005 – Applicants' IDS) teach that the importance of different epitopes of carbohydrate antigens of bacteria and fungal pathogens formed by various chemical substituents in contributing to protective immunity 'can be quite variable'. Kelly-Quintos *et al.* teach of the unpredictable and diverse effect the acetyl groups of a microbial polysaccharide have on pathogenicity and protective immunity. For instance, Kelly-Quintos *et al.* teach that while the removal of the O-acetyl groups from meningococcal C capsular polysaccharide has an effect on the induction of bactericidal antibodies, O-acetyl substituents on the *S. aureus* capsular polysaccharides seem to have no effect on elicitation of opsonic antibody effective against expressing either high or low levels of acetate on the surface capsular polysaccharide antigen. Kelly-Quintos *et al.* further teach that even on the same carbohydrate molecule, several different epitopes can bind opsonic protective antibody. See first full paragraph on page 2018. Clearly, *at the time of the invention*, Applicants were not possession of a representative number of dPNAG species of the recited molecular weight which, with or without conjugation to a generic carrier compound or a protein/peptide carrier, stimulated an immune response against any bacteria, pathogenic or non-pathogenic, that make native PNAG. Contrary to Applicants' argument, Maira-Litran's *post-filing* (2005) disclosure that antibodies reactive with the nonacetylated backbone portion of the PNAG antigen were able to mediate clearance of bacteria from the blood and protection against a high-dose lethal staphylococcal infection does not and cannot show that Applicants' had possession of the whole genus *at the*

time of the invention (11/12/2002). For the reasons delineated *supra*, the rejection stands.

19) The rejection of claims 2, 12, 13, 21, 23, 24, 86-91, 93-95 and 97 made in paragraph 24 of the Office Action mailed 03/06/09 under 35 U.S.C. 102(a) as being anticipated by Yang *et al.* (*Tetrahedron Lett.* 43: 7561-7563, October 2002, of record), is maintained for the reasons set forth therein and herein below.

Applicants state that claims 2, 21 and 86 are amended to recite that the isolated beta-l,6-glucosamine polymer, *optionally* conjugated to a carrier compound, has a molecular weight of at least 1200 Daltons and that Yang *et al.* does not teach a polymer or polysaccharide that is at least 1200 Daltons in molecular weight.

Applicants' arguments have been considered, but are not persuasive.

As set forth previously, Yang *et al.* taught an isolated synthetic (1->6)-beta-D-glucosamine hexasaccharide (i.e., at least 1200 Daltons) composition having bioactivities for *in vivo* use. The prior art (1->6)-beta-D-glucosamine hexasaccharide lacks acetate substitution and therefore meets the instant limitation: less than 40%, less than 35%, less than 5% etc. of the glucosamine amino groups substituted with acetate. The prior art (1->6)-beta-D-glucosamine is a hexasaccharide and therefore meets the instant limitation: 'n is …. at least four', 'n … of at least 6' and therefore necessarily has a molecular weight recited in the instant claims. The pentasaccharide (1->6)-beta-D-glucosamine in the prior art compound is joined or linked to the sixth unit, i.e., a carrier compound. See title; abstract; and the entire document including the last product in Scheme 2. The rejection stands.

New Rejection(s) Necessitated by Applicants' Amendment

Rejection under 35 U.S.C § 112, First Paragraph (New Matter)

20) The following is a quotation of the first paragraph of 35 U.S.C. § 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

21) Claims 1, 2, 21 and 86 and the claims dependent therefrom are rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

Claims 1, 2, 21 and 86, as amended, now recite an isolated polymer having the formula depicted therein and having a molecular weight of at least '1200' Daltons, wherein n is an integer that is at least four. The limitation 'at least four' has a minimal requirement of four. Therefore, the minimally required n in claims 1, 2, 21 and 86 is four. Accordingly, the claimed isolated polymer having the structure depicted therein wherein n=4 has to have a molecular weight of at least '1200 Daltons'. However, there is no descriptive support for such an isolated polymer and a composition comprising the same. The specification at lines 20-24 of page 13 indicates that four monomeric units of the polymer have a molecular weight of less than 1200 Daltons. Therefore, the now claimed polymer in the amended claims is new that lacks support in the as-filed specification. See M.P.E.P 608.04 to 608.04(c).

Applicants are respectfully requested to point to the descriptive support in the specification as filed, by pointing to specific lines and pages, for the new

limitations/scope, or alternatively, remove the new matter from the claim(s). Applicants should specifically point out the support for any amendments made to the disclosure. See MPEP 714.02 and 2163.06.

Rejection(s) under 35 U.S.C § 103

22) The following is a quotation of 35 U.S.C. § 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> **(a)** A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 148 USPQ 459, that are applied for establishing a background for determining obviousness under 35 U.S.C. § 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or unobviousness.

23) Claims 1, 4-7, 10, 11, 14, 15, 18, 20, 42 and 99 are rejected under 35 U.S.C. 103(a) as being unpatentable over Yang *et al.* (*Tetrahedron Lett.* 43: 7561-7563, October 2002, of record) and claims 19 and 96 are rejected under 35 U.S.C. 103(a) as being unpatentable over Yang *et al.* (*Tetrahedron Lett.* 43: 7561-7563, October 2002, of record) as applied to claims 2 and 86 above in paragraph 19 supra.

Yang *et al.* taught a composition comprising distilled water (i.e., pharmaceutically acceptable carrier) and an amount of an isolated synthetic (1->6)-beta-D-glucosamine hexasaccharide (i.e., at least 1200 Daltons) having bioactivities for *in vivo* use. The composition was injected into mice. The prior art

(1->6)-beta-D-glucosamine hexasaccharide lacks acetate substitution and therefore meets the instant limitations of less than 40%, less than 35%, less than 5% etc. of the glucosamine amino groups substituted with acetate. The prior art (1->6)-beta-D-glucosamine is a hexasaccharide and thus meets the instant limitation of 'n is .... at least four', 'n of ... at least 6', and therefore is expected to have a molecular weight recited in the instant claims. The pentasaccharide (1->6)-beta-D-glucosamine in the prior art compound is joined or linked to the sixth unit, i.e., a carrier compound. See title; abstract; Table 1; last full paragraph on page 7562; and the entire document including the last product in Scheme 2. Since the prior art composition is structurally the same as the instantly recited composition, it is expected to have the same functions as that of Applicants' composition, including the ability to stimulate an immune response in a subject as recited in claims 42 and 99.

Yang *et al*. do not expressly disclose that their composition is sterile.

However, rendering an art-known product meant for *in vivo* use sterile was routine and conventional in the art at the time of the invention via a routine art-known sterilization procedure such as sterile filtration or production of the composition under sterile GMP conditions. Given that Yang's composition is meant for *in vivo* use as an antitumor agent, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to render Yang's composition sterile using any art-known sterilization procedure to produce the instant invention. One of ordinary skill in the art would have been motivated to produce the instant invention for the purpose of providing Yang's composition in a sterile form most suitable for the intended *in vivo* administration.

Claims 1, 4-7, 10, 11, 14, 15, 18-20, 42, 96 and 99 are *prima facie* obvious over the prior art of record. Furthermore, the term 'formulated as a vaccine' in

claim 20 represents a process limitation. When claims are drawn to a product-by-process, claims are not limited to the manipulations of the recited step(s), but only the structure implied by the steps. MPEP § 2113 states:

> [E]ven though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process. *In re Thorpe, 777 F.2d 695, 698, 227 USPQ 964, 966 (Fed. Cir. 1985)* (citations omitted).

A product does not have to be made by the same process in order to be the same product, because a product is a product, no matter how it is claimed. The method of formulation does not impart any structural limitation to the product. In the instant case, Applicants have not shown the underlying structure of the prior art composition differs from that of the instantly claimed composition.

24) Claims 16, 17, 25 and 98 are rejected under 35 U.S.C. 103(a) as being unpatentable over Yang *et al.* (*Tetrahedron Lett.* 43: 7561-7563, October 2002, of record) as applied to claims 1, 15 or 21 above, and further in view of Masuho *et al.* (US 4,379,145).

The teachings of Yang *et al.* are explained above. Yang *et al.* further taught that their isolated synthetic (1->6)-beta-D-glucosamine hexasaccharide (i.e., at least 1200 Daltons) having bioactivities for *in vivo* use is a potent antitumor agent. See page 7562. Yang *et al.* do not expressly disclose that their polymer is linked or conjugated to a protein or peptide carrier.

However, it was routine and conventional in the art at the time of the invention to link or conjugate an art-known antitumor agent to a protein or fragment thereof, with or without a liker. For example, Masuho *et al.* taught that an anti-tumor agent is conjugated to a special carrier, such as, an anti-tumor

antibody or a Fab fragment (i.e., peptide) thereof, to make it selectively attractive to tumor cells. See lines 17-54 in column 1 and Examples.

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to conjugate or link Yang's isolated antitumor polymer to an art-known anti-tumor antibody or a Fab fragment (i.e., peptide) thereof to produce the instant invention. One of ordinary skill in the art would have been motivated to produce the instant invention for the purpose of making the antitumor polymer in Yang's composition selectively attractive to tumor cells as taught by Masuho *et al.*

Claims 16, 17, 25 and 98 are *prima facie* obvious over the prior art record.

25) Claim 9 is rejected under 35 U.S.C. 103(a) as being unpatentable over Yang *et al.* (*Tetrahedron Lett.* 43: 7561-7563, October 2002, of record) as applied to claim 1 above.

The teachings of Yang *et al.* are explained above, which do not teach that their synthetic polymer has a molecular weight of at least 1500 Daltons. However, Yang *et al.* expressly taught that their highly efficient and practical procedure can be used to build up more complicated glucosamine oligosaccharides. See first paragraph on page 7563.

Therefore, increasing the length of Yang's synthetic (1->6)-beta-D-glucosamine hexasaccharide by adding two or more repeats of (1->6)-beta-D-glucosamine was well within the realm of routine experimentation, would have been obvious to one of ordinary skill in the art, and would have brought about predictable results.

Claim 9 is *prima facie* obvious over the prior art of record.

Remarks

26) Claims 1, 2, 4-7, 9-21, 23-25, 42 and 86-99 stand rejected.

27) Applicants' amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** Applicants are reminded of the extension of time policy as set forth in 37 C.F.R 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 C.F.R 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

28) Papers related to this application may be submitted to Group 1600, AU 1645 by facsimile transmission. The Fax number for submission of amendments, responses and/or papers is (571) 273-8300, which receives transmissions 24 hours a day and 7 days a week.

29) Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAG or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.Mov. Should you have questions on access to the Private PAA

system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (in USA and CANADA) or 571-272-1000.

30) Any inquiry concerning this communication or earlier communications from the Examiner should be directed to S. Devi, Ph.D., whose telephone number is (571) 272-0854. A message may be left on the Examiner's voice mail system. The Examiner can normally be reached on Monday to Friday from 7.15 a.m. to 4.15 p.m. except one day each bi-week, which would be disclosed on the Examiner's voice mail system.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Larry Helms, can be reached on (571) 272-0832.

/S. Devi/
Primary Examiner
AU 1645

September, 2010